REMARKS

Examiner Interview Summary

Applicants gratefully acknowledge the Interview granted by the Examiner and attended by the undersigned in the Examiner's office on June 26, 2003. While the Examiner prepared an Interview Summary, he did not indicate that it was not necessary for Applicants to provide a separate record of the substance of the interview; therefore, the interview is further commented upon herein.

Several issues were discussed at the interview, which are commented upon in more detail in the Remarks below under the headings for the various issues. Those included:

- The rejection under 35 U.S.C. § 112, first paragraph, which the Examiner explained as resulting from an interpretation of claim 40 which could possibly read on an "isolated" chromosome separated to some degree from the rest of the cell by manual manipulation under a microscope, as well as language in the specification which might be included in the claims to clarify the intended scope of the claims.
- Whether this possible issue is one that supervisors in Technology Center 1600 have considered to be of any concern with respect to patent scope, and whether the requirements made are in conformity with currently policies of TC 1600; the Examiner agreed to discuss this language with his supervisor(s).
- The possibility that the Examiner would consider extending examination to the withdrawn claims, including polypeptide and antibody claims, in addition to claims to methods of making and using the elected polynucleotides which should be rejoined as a matter of right upon allowance of a product claim per the Commissioner's Notice in the Official Gazette of March 26, 1996, entitled "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)" which sets forth the rules, upon allowance of a product claim, for rejoinder of process claims covering the same scope of products. The Examiner agreed that he would consider doing so.
- The newly issued patent (6,518,046) to Human Genome Sciences that contains claims that may interfere with Applicants' claims to PANEC-2.

Comments regarding canceled subject matter and the pending restriction requirement

Polynucleotides encoding the chemokines PANEC-1 and PANEC-2 have been elected and examined. Since filing and examination of this application began over 8 years ago, other Applicants have filed and had issued patents which may conflict with the subject matter of this application. The instant application was suspended for over two years, after which the mentioned application(s) of others was/were allowed and issued, with claims that possibly conflict with claims currently pending in the instant application. Applicants have pursued prosecution of these inventions since the suspension was lifted.

In order to expedite issuance of claims to the invention which most clearly has priority over the similar invention of others, namely the claims directed to PANEC-1, Applicants have elected to pursue the claims directed to PANEC-2 in a copending divisional application, and have canceled claims directed to PANEC-2 herein. Applicants explicitly assert that the cancellation of these claims is not to be construed as an admission of unpatentability of the claims directed to PANEC-2, but rather is in order to expedite prosecution of the invention of PANEC-1 in the present application, as the invention of PANEC-1 has different priority issues, and with a different party, as compared with PANEC-2.

Applicants note that the instant application has been pending since February 1995. Therefore, claims issuing from any divisional or continuation applications will be subject to loss of patent term which is currently almost 8.5 years of the 20 year term of any such divisional or continuation application, even assuming hypothetically that such a patent could be issued immediately. Applicants therefore respectfully reiterate their request that the Examiner consider, upon finding the claims to nucleotides encoding PANEC-1 allowable, extending examination of the instant invention to all of the claims directed to various aspects of PANEC-1, including polypeptides encoded by the elected allowable nucleotides, antibodies that specifically bind the polypeptides, and methods of making and using all of them. It is noted that Applicants have provided the Examiner with a search of the art related to various aspects of both PANEC-1 and PANEC-2, including alignments of the sequences in the various publications submitted in order to reduce any substantial burden on the Examiner that might otherwise be present with respect to such extension of examination.

In any case, Applicants reserve the right to prosecute canceled and non-elected subject matter in concurrent and subsequent divisional applications.

Support for amendments and newly added claims

Amendments to the language "immunogenically active" instead of "immunogenic" are primarily grammatical in nature.

Support for the language "allelic or recombinant variant" added to the claims, e.g., claim 40, can be found on page 8, lines 1-2: "The DNAs which encode PANEC-1 and PANEC-2 may also include allelic or recombinant variants and mutants thereof."

Support for the various limitations in the amounts and types of insertions, deletions and substitutions include mathematical calculations or sequence selections based upon the teaching of the specification, including Fig. 3 (now 3A, 3B and 3C), which compares PANEC-1 to its three closest prior art molecules known at the time of the invention, namely MCP-1, MCP-2 and MCP-3. For example, in the amendments to claim 40, the language "has an insertion or deletion of 1-5 amino acids as compared with SEQ ID NO:2" is supported on page 7, lines 6-7.

Similarly, in the amendments to claim 40, the language "has a substitution of 1-28 amino acids as compared with SEQ ID NO:2," is supported by the language in the paragraph bridging pages 6-7: "may be found by comparing the sequence of the particular PANEC with that of homologous cytokines and minimizing the number of aa sequence changes made in regions of high homology"; by counting the number of amino acid changes between PANEC-1 and MCP-1 (which is the closest in sequence identity of the three MCPs disclosed in the specification) in Fig. 3 (29 amino acid differences with PANEC-1, not counting the extra two amino acids in MCP-1), it is clear that up to 28 amino acid substitutions can be made without reading on the prior art MCP-1. Conversely, in claim 107, the number "68" is the number of residues which must remain the same in this 97 amino acid protein. While support for the integers "28" and "68" are not literally present, Applicants submit that it can be fairly construed by reference to Fig. 3. See the attached sequence comparison of MCP-1 and PANEC-1 (see attached Exhibit J).

A similar comparison can be made between PANEC-1 with respect to all three of the prior art MCPs disclosed in the specification (see attached Exhibit K). Again, the disclosure in the specification in the paragraph bridging pages 6-7, ("may be found by comparing the sequence of the particular

PANEC with that of homologous cytokines and minimizing the number of aa sequence changes made in regions of high homology") provides guidance for and supports identification of specific amino acid residues of PANEC-1 which should be retained in a variant, i.e., wherein 2 of the 3 MCPs ("homologous cytokines") have the same amino acid at a specific location ("minimizing the number of aa sequence changes made in regions of high homology") as PANEC-1, and by only allowing sequence variation at residues where PANEC-1 differs from at least 2 of the 3 MCPs. Those specific sequences where changes should not be made are easily identified with reference to Fig. 3, and are recited in new claims 105 and 106. It is clear that there can be substitutions at the other amino acid positions which can be made without reading on the prior art MCPs. While support for the list of specific amino acid sequences of PANEC-1 which are preferably invariant is not literally present, it also can be fairly construed by reference to Fig. 3.

Drawing Objections

The drawings are corrected by submission of the attached replacement pages. The corrections are all formal in nature, putting the Figures in compliance with margin and font size requirements, and do not contain any substantive amendments. Amendments to the specification have been made to reflect the new Figure numbering.

Title Objection

The title of the application has been amended to be more clearly descriptive of the claimed chemokine polynucleotides, polypeptides and antibodies thereto, and methods of making and using them. While Applicants would be happy to further change the title to include the now art-recognized term "Eotaxin," it is not clear that such would be proper, as the term does not appear in the specification. Clarification of the Examiner's request is earnestly solicited.

New Matter

Applicants note that the Examiner is correct in citing the literal absence of the term "90% identity" in the specification of the above-identified application. Nevertheless, it is clear that Applicants

more than adequately disclosed and intended to claim variants of their sequence. Applicants have now rewritten their claims to include specific references supported in the specification of how and where in the molecules the claimed polypeptides and polynucleotides they encode can differ from the specific sequences disclosed in the specification, as discussed *supra*.

Rejection of claims 40-42, 46 and 47 under 35 U.S.C. § 112, first paragraph

Applicants first respectfully note that the rejection appears to be unclear as to what is the statutory basis for the rejection. The rejection is repeatedly stated as being a failure of "written description enablement"; however, Applicants are not clear from this language whether the rejection is for lack of written description or for lack of enablement, which of course are two separate requirements of 35 U.S.C. § 112, first paragraph.

In the Office Action on page 8, paragraph bridging to page 9, the Examiner states that the rejected claims "are directed to encompass full gene sequences, sequences that hybridize to SEQ ID NOs: 1 or 3."

First, claims to SEQ ID NO:3 are no longer pending in this application, although the following arguments apply equally to the claims to PANEC-2 that have been canceled herein.

Second, the rejected claims do not recite the words "full gene" in describing the claimed polynucleotide sequences, nor do they claim sequences that "hybridize to SEQ ID NO:1." The claim is directed to "*[a]n isolated polynucleotide* comprising a polynucleotide sequence selected from the group consisting of: ... *a polynucleotide sequence encoding an amino acid sequence of SEQ ID NO:2* ...". The plain meaning of the words in the claim, particularly as taken in view of the state of the art (including literally thousands of other gene patents issued by the USPTO that use essentially identical language to the instant claim 40), the disclosure in the specification and the prosecution history over 8.5 years of pendancy of this case make it clear that the claimed sequences do not encompass genomic DNA, nor an isolated chromosome on a microscope slide (as was discussed at the interview on June 26, 2003), said hypothetically encompassed sequences clearly failing to be either useful under 35 U.S.C. § 101 or novel under § 102. Applicants note that in the references cited by the Examiner as

encompassing genomic sequences, such was accomplished by the patentees' express intent to include genomic sequences, which intent is not present herein, either in the specification or file history.

The Examiner (and the courts) are directed by *Genentech Inc v. The Wellcome Foundation Ltd.*, 31 USPQ2d 1161(Fed. Cir. 1994) to construe claims in such a way as to preserve validity, particularly when there is only one reasonable way of construing the claims asserted by Applicants during prosecution. As the Federal Circuit said:

> An appropriate method for resolving the issue [the proper scope of the phrase "human tissue plasminogen activator" appearing in the claims] is to avoid those definitions upon which the PTO could not reasonably have relied when it issued the patent. That is an appropriate method to follow because it avoids the possibility of an applicant obtaining in court a scope of protection which encompasses subject matter that, through the conscious efforts of the applicant, the PTO did not examine. An applicant should not be able deliberately to narrow the scope of examination to avoid during prosecution scrutiny by the PTO of subject matter with the objective of more quickly obtaining a patent (or avoiding the risk of an estoppel), and then obtain in court, either literally or under the doctrine of equivalents, a scope of protection which encompasses that subject matter. See *North American Vaccine Inc.*, 7 F.3d at 1577, 28 USPQ2d at 1337. [footnote omitted]

Applicants expressly assert that the Examiner's concern that the scope of Applicants' claims might be extended, by torturous claim construction, to include genomic and/or chromosomal sequences not supported in the specification is therefore misplaced, as Applicants have clearly not only disclaimed it by the plain meaning of the claims, but also expressly herein as well as in previous prosecution papers. No court or member of the public could reasonably read them so broadly.

In any case, Applicants have proposed alternative claim language, supported by the specification and the knowledge of those of skill in the art, in claim 107 ("non-genomic," supported as the negative of the definition in the specification on page 10, lines 23-25, of genomic sequences as "including promoters, enhancer elements and introns of the respective naturally occurring panecs"), and in claim 108 ("encodes, without introns," supported in the same place in the specification). For the record, Applicants submit herewith a printout from NCBI ("AceView") of the human gene encoding CCL11, which is identical to the PANEC-1 gene, showing that it comprises 3 exons as it occurs naturally on chromosome 17. Clearly, the instant claims do not encompass the sequence as it occurs in nature.

Further Comments on Enablement of Protein/Antibody Claims and Methods of Use

Upon determination of allowability of the polynucleotide claims, Applicants have requested rejoinder of all of the pending claims related to the core invention of PANEC-1, including polypeptides, antibodies that specifically bind to the polypeptides and methods of use of all of the compositions of matter.

In further support of this request, Applicants submit herewith (1) various pages from Cambridge Antibody Technology's website, disclosing their therapeutic use of antibodies (CAT-213) to eotaxin (PANEC-1) for treatment of human allergic disorders; and (2) a May 19, 2003, press release from the Yahoo! Finance website, discussing (page 3 of 15) that recruitment of patients for the Phase I/II allergen challenge study of Cambridge Antibody Technology's CAT-213 was completed.

Still further, Applicants have attached a copy of a report from the IDdb3 database (Investigational Drugs database) (http://www.iddb3.com/), a proprietary database to which Applicants subscribe, disclosing details of the clinical status of CAT-213.

Applicants submit that utility of the antibodies to the PANEC-1 protein encoded by panec-1 polynucleotides, as well as methods of using same, has been clearly demonstrated, and that they should also be allowed.

Prior Art Rejections

Applicants note that the pending rejection of claims relating to PANEC-2 under 35 U.S.C. § 102(e)(2) over Li et al., newly issued, are obviated by the cancellation of this subject matter in favor of continuing prosecution in a continuation application. Again, this cancellation is not to be construed as an acquiescence to the rejection, but is being done in the interest of expediting prosecution of the instant claims directed to PANEC-1, which has different priority issues.

Applicants note that the claims to human eotaxin (i.e., PANEC-1) issued to Luster et al. (6,403,782) appear to have been issued prematurely, in view of Applicants' broader claims to this invention. Luster et al. claim a priority date (June 22, 1995; USSN 60/000,449) over four months after Applicants' priority date of February 17, 1995.

Luster et al. have several claims in their application that are encompassed by the broader claims of the instant application, including:

> 3. Substantially pure DNA encoding the amino acid sequence of SEQ ID NO:27.
> 6. A purified DNA having the nucleotide sequence shown in SEQ ID NO:26.
> 7. The DNA of any one of claims 1, 2, 3, 4, 5, or 6, wherein said nucleic acid is cDNA.
> 8. A vector comprising the DNA of any one of claims 1, 2, 3, 4, 5, 6, said vector being capable of directing expression of the peptide encoded by said DNA in a vector-containing cell.
> 11. Substantially pure nucleic acid encoding the human eotaxin polypeptide of SEQ ID NO: 27.

These claims are encompassed, *inter alia*, by Applicants' pending claims as follows:

> Claim 40 (and claims dependent thereon): Luster claims 3 and 11;
> Claim 52 (and claims dependent thereon): Luster claims 6 and 11;
> Claims 111 and 112: Luster claim 7;
> Claim 35: Luster claim 8.

Applicants respectfully submit that, while not acquiescing to any arguable assertion that Luster et al.'s claims are novel or unobvious over the claims of the instant application (which assertion is in fact not correct), nevertheless, there is no requirement that the Director of the USPTO declare an interference between the allowable claims of the instant application with the claims of Luster et al. 6,403,782, because the claims of Luster et al. fail the USPTO's "two-way test" for whether a USPTO interference should be declared, which test was affirmed by the Court of Appeals for the Federal Circuit in *Eli Lilly & Co. v. Board of Regents of the University of Washington*, (Fed. Cir. Case No. 02-1610 [Interference No. 104,733], decided July 3, 2003):

> If the interference proceeding, however, leads to a conclusion that the genus claim was invented first, it is possible that both the genus and the species are separate patentable inventions. Thus, the Director's two-way test avoids the proliferation of unnecessary, wasteful interference proceedings concluding that both parties are entitled to patents in situations in which the claimed inventions do not define the same patentable invention, but merely overlap in scope. This is the clear application of discretion that is inherent in the authority granted pursuant to 35 U.S.C. § 135(a) of the statute.

Applicants therefore respectfully submit that no declaration of interference with 6,403,782 is necessary in the present application, and request that all claims found to be allowable be passed to issue as quickly as possible. If in fact there is interfering subject matter between the allowable claims of the instant application and the '782 patent, that can be determined by the courts.

Newly Discovered "Art"

The Examiner's attention is directed to the NCBI webpages attached herewith and previously cited on the PTO Form 1449 filed June 2, 2000, regarding sequence gi1552241 (aka BAA08370) and gi1552240 (aka D49372). According to the webpages, this sequence was "submitted" on February 15, 1995, by Osamu Yoshie, Shionogi Institute for Medical Science, Osaka, Japan, two days before the instant application was filed. However, none of the NCBI records (also attached to the webpages) show that it was publicly available on that date, nor even in that year. Applicants sent an email to DDBJ, the Japanese database equivalent to NCBI, to check the possibility that it might have been made publicly available on their database before it was available on NCBI. Their reply (copy attached) states that the sequence became publicly available on May 11, 1996. Therefore, it is submitted that this possible reference in fact is not available as prior art, and is submitted merely to complete the record.

References not considered

The Examiner stated that some references listed on Applicants' PTO 1449 forms, submitted with the previous response, were lined through and not considered, either because dates of publication were not provided, or because the reference was a duplicate of a previously submitted reference. Applicants will be happy to resubmit references that were not considered because the PTO 1449 form was missing the publication date, but Applicants could not find such a lined-through reference on the copy of the 1449, on which almost every reference was initialed, that was returned with the instant Office Action. If the Examiner would clearly point out which references were deficiently presented, Applicants will resubmit them immediately.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that the present application is fully in condition for allowance, and request that the Examiner withdraw the outstanding objections and rejections. Early notice to that effect is earnestly solicited.

If the Examiner contemplates other action, or if a telephone conference would expedite allowance of the claims, Applicants invite the Examiner to contact the undersigned at the number listed below.

Please charge Deposit Account No. **09-0108** in the amount of **$**_____ as set forth in the enclosed fee transmittal letter. If the USPTO determines that an additional fee is necessary, please charge any required fee to Deposit Account No. 09-0108.

Respectfully submitted,

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